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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,543	01/17/2002	David E. Lam		7769

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EXAMINER	
RAO, MANJUNATH N	
ART UNIT	**PAPER NUMBER**
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/914,543	LAM ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-9,14-16,18-20,22-27,29,31,32,35-39,44-55 and 60-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,2,4-9,14,24-27,29,37-39,53-55,62-64,69 and 71* is/are allowed.

6)☒ Claim(s) *15,16,18,20,22,31,32,44-52,60,61,65-68,70 and 72-74* is/are rejected.

7)☒ Claim(s) *19, 23, 35-36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4-11-07 has been entered.

Claims 1-2, 4-9, 14-16, 18-20, 22-27, 29, 31-32, 35-39, 44-55, 60-74 are currently pending and are present for examination. Applicants' amendments and arguments filed on 4-11-07, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Examiner notes the applicants are claiming both the polypeptide and its encoding polynucleotide sequences. However, applicants have filed claims drawn to the method of use of the polypeptides which in actuality is the method of use of the polynucleotide, for example claims 63 and 64. Such claims are highly confusing and unnecessarily take more time to examine. Examiner requests applicants to claim methods of using the polypeptide and method of using the polynucleotide separately so that claims can be examined without any confusion.

Claim Objections

Claims 19 and 35-36 are objected to because of the following informalities: Duplicate claims. Applicant is advised that should claim 19 be found allowable, claim 35 (and claim 36

depending therefrom) will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 20 recites the limitation "synthetic or recombinant polypeptide of claim 19" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. Claim 19 is actually drawn to a nucleic acid of claim 37. Correction is required.

Claims 45-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims depend from the method of claims 15 or 16. These claims recite that the polypeptide is employed in various industries. It is not clear to the Examiner as to how this fits well in the methods of claim 15 and 16. Perhaps applicants intended to recite the activity of the polypeptide than the place where the enzyme is employed. The claims as written does not make any scientific or legal sense.

Claims 49-52, 65-67, 72-74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are drawn to a polypeptide further comprising various things such as a textile, a biomass, a juice etc. The claim as written does not make scientific or practical sense to the Examiner. It is not clear as to how the polypeptide can further comprise a textile. Examiner urges applicants to either cancel the claims are re-write in such a way that it provides a scientific meaning.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor Of carrying out his invention.

Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 18 is drawn to a polypeptide encoded by a nucleic acid sequence which is at least "97%" identical to the nucleotide sequence of any of SEQ ID NO:45. However, a perusal of the specification indicates that applicants have no support for "97% identity to the polynucleotide of SEQ ID NO:45" which now constitutes a "new matter". Therefore claim 18 is rejected for introducing "new matter" into the claims.

A perusal of the specification provides support for per cent identity to polynucleotides on page 20 (reproduced here). While the specification provides direct support for a

Thus, the present invention is directed to polynucleotides having at least a 70% identity, preferably at least 90% identity and more preferably at least a 95% identity to a polynucleotide which encodes the enzyme of SEQ ID NO:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 36, 38, 40, 42, 44, 46, or 48 as well as fragments thereof, which fragments have at least 30 bases and preferably at least 50 bases and to enzymes encoded by such polynucleotides.

The present invention further relates to a enzyme which has the deduced amino acid sequence of Figure 1, as well as fragments, analogs and derivatives of such enzyme.

The terms "fragment," "derivative" and "analog" when referring to the enzyme of Figure 1 means a enzyme which retains essentially the same biological function or activity as

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polynucleotide that is 70%, 90% or 95% identical to SEQ ID NO:45, there is no support for a polynucleotide that is 97% identical to SEQ ID NO:45. Therefore the above rejection is maintained.

Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 22 is drawn to a polypeptide which is at least "97%" identical to the polypeptide sequence of any of SEQ ID NO:46. However, a perusal of the specification indicates that applicants have no support for "97% identity to the polypeptide of SEQ ID NO:46"

which now constitutes a "new matter". Therefore claim 22 is rejected for introducing "new matter" into the claims.

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The enzymes of the present invention include an enzyme of Figure 1A-1X (in particular the mature enzyme) as well as enzymes which have at least 70% similarity (preferably at least 70% identity) to an enzyme of Figure 1A-1X and more preferably at least 90% similarity (more preferably at least 90% identity) to an enzyme of Figure 1A-1X and still more preferably at least 95% similarity (still more preferably at least 95% identity) to an enzyme of Figure 1A-1X and also include portions of such enzymes with such portion of the enzyme generally containing at least 30 amino acids and more preferably at least 50 amino acids.

A perusal of the specification provides support for per cent identity to polypeptides on page 22 (reproduced above). While the specification provides direct support for a polypeptide that is 70%, 90% or 95% identical to SEQ ID NO:46 (referred to sequences in the figure), there is no support for a polypeptide that is 97% identical to SEQ ID NO:46. Therefore the above rejection is maintained.

Claims 31-32, 68, 70, 60-61, 15-16, 44-52, 72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an endoglucanase having the amino acid sequence SEQ ID NO:46 or a polypeptide having 95% amino acid sequence identity to SEQ ID NO:46 and having endoglucanase activity, encoded by a polynucleotide having the nucleotide sequence SEQ ID NO:45 or 95%, nucleotide sequence identity to SEQ ID NO:45 or a nucleotide sequence that hybridizes to SEQ ID NO:45 under stringent conditions and wherein such polynucleotide has 97% sequence identity to SEQ ID NO:45, vectors and host cells

comprising said polynucleotide, does not reasonably provide enablement for any such polypeptide that has 90% sequence identity to SEQ ID NO:46 or a polypeptide encoded by a polynucleotide that has only 90% sequence identity with SEQ ID NO:45, vectors and host cells comprising said polynucleotides and method of making and using said polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 31-32, 68, 70, 60-61, 15-16, 44-52, 72 are so broad as to encompass any variants and fragments of SEQ ID NO:46 or any endoglucanase polypeptide that has 90%, sequence identity with SEQ ID NO:46 or polypeptides encoded by any polynucleotide having a nucleotide sequence which is 90% identical to SEQ ID NO:45 or any polynucleotide having a sequence that is at least 90% identical to SEQ ID NO:45, vectors and host cells comprising said polynucleotides and method of making said polypeptides. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides and polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain

the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single endoglucanase. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides and polynucleotides. The specification is limited to teaching the use of SEQ ID NO: 45 and 46 as a endoglucanase but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495,), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. The specification does not support the broad

scope of the claims which encompass all modifications and fragments of any endoglucanase polypeptide and polynucleotide encoding the same because the specification does not establish: (A) regions of the protein structure which may be modified without affecting its activity; (B) the general tolerance of endoglucanases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including endoglucanases with an enormous number of amino acid modifications to SEQ ID NOS:46. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptide having endoglucanase activity and the polynucleotides encoding the same is unpredictable and the experimentation to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants have traversed the above rejection and continue to argue at length that the specification enables those skilled in the art at the time the invention was made to identify and make and use a genus of polypeptides having endoglucanase or cellulase activity and the nucleic acids that encode them to practice the claimed invention. Applicants refer back to their previous arguments. Examiner respectfully disagrees

that such arguments are persuasive to overcome the above rejection for the very same reasons that he laid down in the previous Office actions.

In summary (considering the previous applicant's arguments), applicants maintain that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, the genus of polypeptides, regarding making mutants or variants using a given sequence of a endoglucanase. Examiner has indeed considered Dr. Short's Declaration and the previous arguments. In essence, Applicants argue that the rejection under 35 U.S.C. §112, first paragraph is not proper because the specification teaches the complete sequence of the enzyme, and protocols for testing enzymatic activity, and methods for producing variants of a disclosed sequence are within the skill of the ordinary artisan. Applicants argue that while the number of samples needed to be screened may be high, the procedures are routine and yield successful results. Applicant also argues that screening large numbers of composition --as long as the screening is routine--, is irrelevant to enablement and reiterates a court decision handed down. Examiner respectfully disagrees with all the above arguments. Referring to the Office's argument of lack of guidance to make the mutants and variants, applicants maintain that the specification and level of knowledge to the skilled artisan was more than enough guidance to satisfy enablement requirement.

Applicants maintain the argument that the skilled artisan using the teaching of the specification had sufficient (reasonable) guidance as to what base or amino acid substitutions could have been made to make the genus of endoglucanases of the invention (e.g., what amino acid substitutions could have been made to make the genus of glycosidase enzymes of the invention), that information was, *inter alia*, readily available in the form of endoglucanase

sequences known in the art at the time of the invention. Applicant maintains that a routine, simple sequence alignment comparison of known glycosidase sequences would have identified regions of identity and dissimilarity to provide guidance to the skilled artisan as to which sequences could be changed, or not changed, to generate structural and/or functional variations of an exemplary endoglucanase. With such information, applicant argues, that if one skilled in the art desired some structural guidance as to what amino acid substitutions could be made to make the genus of endoglucanase of the invention, such guidance could be found both in the specification and the state of the art at the time of the invention. Examiner respectfully disagrees with such a line of argument. This is because, irrespective of whatever guidance provided in the specification or in the art, one of ordinary skill in the art will be subject to undue experimentation in order to arrive at active polypeptides having glycosidase activity at said per cent homology. Although the claims are not limited to variants having only a single amino acid substitution, in order to generate only single amino acid variant of SEQ ID NO:46, one must make 19^{319} just for making single amino acid variants. This number was determined by recognizing that SEQ ID NO:46 is 319 amino acids in length. Because there are 19 other possible naturally occurring L-amino acids that can replace each amino acid of SEQ ID NO:2, the number of possible variations is 19^{n} , where n = number of amino acids in a polypeptide. Thus, for only single amino acid substitution, the number of variants is 19^{319} and the number becomes seemingly infinite when one considers that the claims broadly encompass simultaneous alteration of substitution, addition, deletion, and/or insertion of up to 31 amino acids (for 90% sequence identity) in a polypeptide that is 319 amino acids in length. Based on this rough approximation, the number of allowed permutations is astounding. While methods to produce variants of a known sequence,

site-specific mutagenesis and random mutagenesis, are well-known to the skilled artisan, producing variants having glycosidase activity requires that one of skill in the art know or be provided with guidance for the selection of which of the at least 19^{319} variants has the desired activity. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the at least 19^{319} possible variants. Current techniques (*i.e.*, high throughput mutagenesis and screening techniques) in the art would allow for finding a few active mutants within several hundred thousand or up to about a million inactive mutants as is the case for the claims limited to 95% identity (despite even this being an enormous quantity of experimentation that would take a very long time to accomplish) but finding a few mutants within several billion or more as in the claims to 90% identity would amount to undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. Hence the above rejection is maintained.

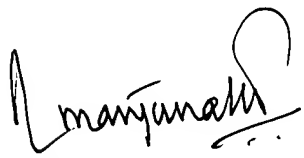
Conclusion

Claims 1-2, 4-9, 14, 24-27, 29, 37-39, 53-55, 62-64, 69, 71, 73-74 are allowable.

Claim 23 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

June 14, 2007